Check list for documents of new biological products registration file

Date of Submission	
Product Name	
Applicant Name	
Applicant Representative	
Biological Registration Specialist	

	Prepare 6 separate files as follows	Check	Notes
	File I: Core Registration file		
	First: Administrative data		
1	**Applicant profile submitted & updated**		
2	**Index**		
3	**Covering letter on applicant head letter signed and stamped by the registration general manager for file submission for registration**		
4	**Copy of Inquiry approval**		
5	**Copy of pricing certificate or proof of pricing file submission in case of reliance or fast track pathway**		
6	**C.D. containing all content of the 5 files (core, inspection, quality,stability, scientific & PV)**		
7	**A certification that all data in the file is true and accurate and updated and identical to the CD**		
8	**Copy of all approvals or Exemptions related to the Product (technical committee, scientific committee, inspection reports, …)**		
8	**Copy of Authorization letter for the person responsible for communication on behalf of applicant during the procedure andthis letter should be certified as truly signed**		
9	**Payment receipt (according to last update of fees decree)**		
10	**Application form for registration of biological medicinal productsSigned & Stamped by the Applicant (each paper)**		
11	**Composition Certificate**		
	Original		
	Authenticated & Notarized (if not attached to CPP) * for imported products		
	On license holder letter head		
	Signed & Stamped by the license holder		

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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

	Trade name of the product is specified		
	Dosage form of the product is specified		
	Active ingredient (s) with its (their) quantity (ies) per unit dose is (are) specified		
	inactive ingredient (s) with its (their) quantity (ies) per unit dose is (are) specified		
	Specifications of Active & inactive ingredients are mentioned (e.g. in house specification , USP ,EU ,JP ,British pharmacopeia)		
	The overage should be mentioned		
	Identical to CPP & CTD		
	API name is specified (the INN, scientific, pharmacopoeia, common name accompanied by its salt orhydrate form (if any))		
12	**<u>For Imported products:</u> CPP issued by Competent Authorities inCountry of Origin**		
	Original		
	Authenticated from Embassy		
	Valid		
	The Arab Republic of Egypt is mentioned as Importing Country		
	Number of product license is specified		
	Date of issue is specified		
	Dosage form (s) and Strength (s) are specified.		
	License Holder (address, city, country) is specified		
	Role of License Holder is specified		
	Manufacturer of solvent should be mentioned (if different from manufacturer of the finished product)		
	Product marketed in the COO		
	Manufacturing sites involved in the manufacturing of the product should be mentioned with its role (Finished product, Primary Packager, Secondary Packager, Batch releaser, Solvent manufacturer)		
	Good Manufacturing Practice (GMP) of the manufacturer is specified		
	Pack Presentation and pack size(s) of the Product is (are) specified (could be as an attachment)		
	Active Ingredient(s) by its salt or hydrate form (if any) with its (their) quantity (ies) per unit dose is (are)specified		
	Inactive Ingredient(s) with its (their) quantity (ies) per unit dose is (are) specified (could be as an attachment)		
	Shelf-life of the Product is specified (could be as an attachment)		
	Storage Conditions of the Product is specified (could be as an attachment)		
	SPC or package insert of the product (could be as an attachment)		
	If the Name of the product may change in Egypt, copy of CPP from any reference country with the name targeted to be in Egypt should be submitted (technical committee decision on 22/5/2014).		
13	**GMP of all the manufacturers involved in the productionprocess** **(Manufacturer of active substance, Manufacturer of finished, Manufacturer of solvent, primarypackager, Secondary packager and Batch Releaser)**		
	Authenticated (From Embassy) original or true copy (authentication on the certificate)		
	Valid		

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	The name of plant by its address should be specified		
	The date of the last inspection should be specified		
	The invalidation date should be mentioned		
	The production lines are specified		
14	**Copy of Manufacturing license for <u>All manufacturing sites</u>**		
	Valid		
	Authenticated (From Embassy) original or true copy (authentication on the certificate)		
	The name of plant by its address should be specified		
	The invalidation date should be mentioned		
	The production lines are specified		
	Issued from the health authority of the specified country		
15	**TSE/BSE free declaration for products contain animal-derived materials used at any stage in the manufacturing**		
	Original letter from the company mentioning that Product is TSE free and mentioning Countries of origin of source materials		
16	**Certificate of suitability (applicable in case the presence ofanimal materials susceptible to transmit TSE) if Not applicable: Supplier official declaration(s) stating thesafety of the substances used in the product manufacturing**		
17	**<u>In cases of imported bulk products and packing in local manufacturing site:</u>** the packaging contract between the foreign manufacturing company and the local packaging site should Submitted		
18	**<u>In case of Toll manufacturing:</u> the manufacturing contract specifying the intended product should be submitted should becertified as truly signed**		
19	**<u>For Imported products:</u> List of the countries where the product is registered & marketed including trade name in each country & marketing status:** Should be notarized from the chamber of commerce or its equivalent in the country of origin and certified from the Egyptian embassy abroad		
20	**Outer label of the Product (1 original pack and 7 layouts)**		
	Trade Name is typed in the same way and style (identical to the CPP, approved insert or SPC & stability approval)		
	The Pharmaceutical dosage Form (identical to the CPP)		
	Composition of all inactive ingredients (as mentioned on the pack of the COO)		
	Active ingredients or generic name with their quantities or strengths are mentioned on the Outer pack(identical to the CPP, approved insert or SPC & stability approval)		
	Manufacturer of the finished product & solvent (if needed) with their address		
	Route of administration (e.g.: IV, IM. SC, infusion…)		
	Concentration (with equivalence).		
	If the dosage form or the product is related to special population (infant, Children, adults), it should be mentioned on the pack		

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	Different concentration should have different printing color for easier identification		
	Number of Units of the dosage form present in the container or inquiry approval (as pricing approval)		
	Batch number is mentioned on the Outer pack		
	Manufacturing date is mentioned on the Outer pack		
	Expiry date is mentioned on the Outer pack		
	Storage conditions are mentioned on the Outer pack (as stability approval)		
	Warning for all drugs "Keep out of reach of children" must be mentioned / & In case of presence of some ingredients (for exp.: Aspartame. Sunset yellow, Benzalkonium chloride, Benzyl alcohol andothers) they should be mentioned		
	English speaking pack (in addition to Arabic language in case of local products)		
21	**Inner Label of the product (1 original label and 7 layouts)**		
	The manufacturer should be specified		
	The trade name		
	Generic Name with strength		
	Batch number is specified		
	Manufacturing date is specified		
	Expire date is specified		
22	**Official declaration (from scientific office or from manufacturer)stating the type of the submitted pack (COO pack , country- specific pack , international pack …..etc.) with differences**		
23	**Official declaration stating the relationship between Manufacturer, Importer and Distributor that Should be notarized from the chamber of commerce or its equivalent in thecountry of origin and Authenticated from the Egyptian embassyabroad**		
24	**Copy of Agency or distribution contract that Should be notarizedfrom the chamber of commerce or its equivalent in the country oforigin and Authenticated from the Egyptian embassy abroad & submit original for review**		
25	**<u>In case of imported bulk naked vial</u> that manufactured abroadand packed locally, the following is required:** - **Copy of packaging contract between the importing company &local manufacturing** - **Original Authorization letter from the abroad mother companyto the importing for product registration and packaging with a local licensed packaging site (Should be notarized from the chamber of commerce or its equivalent in the country of origin and Authenticated from the Egyptian embassy abroad & submit original for review)**		

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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

26	**Letter of Acknowledgment of full responsibility for storing theraw materials and for all stages of manufacturing and for the product's conformity with the technical specifications until thecompletion of distribution**		
27	**Submitting a pledge acknowledging his commitment to the provisions of the Intellectual Property Protection Law No. 82 of2002**		
28	**- Submit the updated scientific office license, importer register for all importers, Updated Storage License for all Storage sites, updated Tax card & Commercial register** **- List of distributors for the submitted product in Egypt mentioning the responsibility for Lot release activity.**		
29	**Product insert**		
Second: Ingredients & packaging materials			
A) Active ingredients:			
30	**Specifications of the active ingredients and the relevant tests.**		
31	**Certificate of Analysis (one COA for each manufacturing site)**		
	Original		
	Signed by the Company or the concerned center or laboratory that held the analysis		
	Stamped by the Company or the concerned center or laboratory that held the analysis		
	Product name, strength and form are specified		
	Manufacturing date is specified		
	Expiry date is specified		
	Batch number is specified		
B) Excipients:			
32	**Specifications of the inactive ingredients and the relevant tests.**		
33	**Certificate of Analysis**		
	Signed by the Company or the concerned center or laboratory that held the analysis		
	Stamped by the Company or the concerned center or laboratory that held the analysis		
	Product name, strength and form are specified		
	Manufacturing date is specified		
	Expiry date is specified		
	Batch number is specified		
34	**Supplier name & origin**		
35	**If the blood derivatives as excipients the company submit:** - plasma source certificate - HIV-1, HIV-2, HBsAG, HCV freedom certificate for the plasma **<u>If the blood derivative manufacturer is not approved in Egypt</u> a commitment letter that the supplier for blood derivate will**		

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	inform the applicant with any information related to safety andefficacy of the product		
C) Finished product			
36	**Specifications of the finished product and the relevant tests**		
37	**Certificate of Analysis of finished products for each manufacturing site (if present)**		
	Original & valid while submission		
	Signed by the Company or the concerned center or laboratory that held the analysis (**Authenticatedand Notarized**)		
	Stamped by the Company or the concerned center or laboratory that held the analysis		
	Product name, strength and form are specified		
	Manufacturing date is specified		
	Expiry date is specified		
	Batch number is specified		
38	**COA of solvent for each manufacturing site (if present) Authenticated and Notarized)**		
39	**CD containing Complete & updated CTD**		
40	**In case of reliance products (level 2 file submission), the following are generally required:** 1- Complete CTD file, with detailed SOPs, the dossier should be the same as that submitted to the reference drug regulatory agency for modules 2-5 2- all annexes and appendices related to safety and efficacy issues of the product with full details 3- a declaration letter by the product owner/applicant stating that all aspects of the product's quality, safety and efficacy are identical to the currently approved by the reference agency with the same dose, indication, warnings and precaution.		
41	**In case of reliance products (level 1 file submission), the following are required:** 1- full assessment report along with other relevant supporting documents from the reference regulatory agency such as: reports pertaining to post-approval variations, post marketing commitments, supporting documents on comparative safety and efficacy studies submitted to the reference agency 2- questions & answer documents between applicant and the reference agency with all annexes 3- any correspondences between the applicant and the reference agency relating to safety and efficacy or queries, the risk management plan, or benefit-risk decisions should be provided		
42	**If the materials entering in the product formulation are from blood derivatives, the following will be presented:**		
	Plasma Master file that contain information of plasma source starting from collection passing all production process & in- process control & Viral safety		
	Official certificates declaring plasma source (legalized in case of blood products active substance)		
	HV-1,HV-2,HBsAG,HCV freedom legalized certificate for the plasma		
	Copy of Certificate of release from Health authority (Drug substance only)		
File II: Inspection file			
1	**Site master file (for Manufacturer of active substance, Manufacturer of finished, Manufacturer of solvent, primary &secondary packager and batch releaser) including:**		

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	•Covering letter from the License holder declaring that the submitted SMF is the most updated andapproved signed, stamped and Authorized •Relevant Premises & utilities information about each site. •Current status of the manufacturing site(s) with respect to current good manufacturing practice (cGMP)requirements. •Legible color printouts of water treatment and air-handling systems, including pipeline andinstrumentation drawings in A3 or A2 format. •List of all the products and dosage forms manufactured on- the same site especially same productionlines.		
2	**GMP of all the manufacturers involved in the production process & Manufacturing license indicating production lines (Active substance, Manufacturer of finished, Manufacturer of solvent, primary packager)**		
3	**- <u>The following documents will be submitted if applicable:</u> Latest full inspection report(s) for inspection performed by a stringent regulatory authority in the past three years and their outcomes. -Last Annual product review. -One completed batch manufacturing and packaging record. -List of any recalls in the past three years related to products with quality defects (if found). -Any warning letter or equivalent regulatory action (production- line specific) (if found).**		
4	**CPP of the product**		
5	**Manufacturing process for Active substance and Finished product (and solvent, if present)**		
6	**Manufacturing process validation for Active substance and Finished product (and solvent, if present)**		
7	**Cold chain Storage & transportation procedures.**		
8	**List of each site where the product (Drug Substance and Drug Product), if authorized, is or would be manufactured.**		
9	**Copy of inquiry approval**		
10	**Copy of application form for biological products**		
	File III: Quality file		
1	**Copy of inquiry**		
2	**Copy of application form for biological products**		
3	**Summary protocol (for blood products & vaccines)**		
4	**Detailed SOPs of analytical procedures of the finished product**		
5	**Complete CTD**		
6	**Certificate of Analysis for Drug substance & Finished product &solvent (if solvent present)**		
7	**Any EDA approval or exemption for the concerned product as supporting documents (example: technical committee approvals,Scientific approvals, inspection approvals for non-reference country manufacturing sites,……)**		
8	**Add the sections No. 40 & 41 mentioned in core file section**		
9	**In case of reliance products (level 1 file submission), the following are required:** 1- Full assessment report along with other relevant supporting documents from the reference regulatory agency such as: reports pertaining to post-approval variations, post marketing commitments, supporting documents on comparative safety and efficacy studies submitted to the reference agency 2- Questions & answer documents between applicant and the reference agency with all annexes 3- Any correspondences between the applicant and the reference agency relating to safety and efficacy or queries, the risk management plan, or benefit-risk decisions should be provided **In case of reliance products (level 2 file submission), the following are required:**		

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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

	1- Complete CTD file, with detailed SOPs, the dossier should be the same as that submitted to the reference drug regulatory agency for modules 2-5 2- All annexes and appendices related to safety and efficacy issues of the product with full details 3- a declaration letter by the product owner/applicant stating that all aspects of the product's quality, safety and efficacy are identical to the currently approved by the reference agency with the same dose, indication, warnings and precaution.		

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التـــلـيـــفـــون: ٠٢٣٧٤٨٤٩٨٨

File IV : Stability Dossier Documents			
A. Requirements of Stability file for Imported Biological Products			
	Administrative documents		
1	**Service consideration (except reliance pathway)**		
2	**Summary sheet (Word + signed & stamped PDF)**		
2	If temperature storage is at (25 °C), a commitment from the applicant to store the product in warehouses and pharmacies at temperature not exceeding (25 °C) is required.		
3	If there are any differences regarding the shelf-life and/or storage conditions in the submitted stability file then: a declaration signed & stamped from MAH clarifying the required shelf-life, storage conditions, in-use, after reconstitution and dilution, incompatibilities and precautions for handling is needed. (The declaration must be legalized in case of imported products from non-reference countries)		
4	**Composition:** • Composition from the C.T.D section "3.2.P.1" - It should be similar to Composition in C.P.P. - If the composition isn't present in C.P.P, so legalized composition isrequired. - Signed & stamped composition on company papers - Mentioning trade name, dosage form, strength - It should include a table that contain: (Function, reference to standard & grades (if applicable) of each ingredient)		
5	Stability testing site: If not stated in Manufacturers section in CTD or if more than one stability testing site is mentioned then a signed & stamped declaration from the MAH/manufacturer clarifying the stability testing site is required.		
6	Stability testing site: If not stated in Manufacturers section in CTD or if more than one stability testing site is mentioned then a signed & stamped declaration from the MAH/manufacturer clarifying the stability testing site is required.		

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B. Requirements for the drug substance			
13	**Certificate of analysis (C.O.A) of recently manufactured drugsubstance (manufacturing date within 5-10 years):** - Clarifying the manufacturer name & address, With manufacturing & expiry dates (corresponds to the required shelf life)and tested parameters following the same specifications as in section "3.2.S.4.1".		
14	**Stability studies:** - Stability studies (Long-term & accelerated) & its protocol of 3 (pilot or production scale) batches carried out in the intended drug substance container-closure system, containing manufacturing site, manufacturing date and tested parameters that follows the same specifications as in section"3.2.S.4.1".		
15	**N.B:** - If the Active substance has more than one manufacturer, stability studies must be submitted from each manufacturer. - Pilot scale batches can be provided with an undertaking by the MAH/manufacturer to place the first three production scale batches into the long-term stability program after approval and submitting the study once completed mentioning the date of submission in the undertaking and batch numbers (in case of on-going stability on production batches). - The stability protocol used for studies on production scale batches shouldbe the same as that for the pilot batches, unless otherwise scientifically justified. For imported products from non-reference countries only: Assay chromatograms should be submitted for each time point (in case of HPLCanalysis) or (last time interval by HPLC in case of any other method of analysis) for all batches included in all stability studies - For imported products from non-reference countries only: Assay chromatograms should be submitted for each time point (in case of HPLC analysis) or (last time interval by HPLC in case of any other method of analysis) for all batches included in all stability studies		
C. Requirements for the drug product:			
16	Certificate of analysis "C.O. A" of recently manufactured **finished product** (5-10 years): - Signed and Stamped - Clarifying the manufacturer and primary packager. - With manufacturing & expiry dates (corresponds to the required shelf life)and tested parameters that follows specifications as in CTD section "3.2.P.5.1". - If the product is powder: the color of powder before & after reconstitutionshould be mentioned in the COA and specifications, unless otherwise scientifically justified.		
17	Certificate of analysis "C.O. A" of recently manufactured **solvent** (5-10years), if applicable.		

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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

18	Stability studies: - **Long-term stability** study & its protocol of 3 (pilot or production scale)batches - **Accelerated stability** study & its protocol of 3 (pilot or production scale)batches - **In-use** :(after reconstitution / after dilution) stability study on at least twopilot scale batches (The age of one batch is at the beginning of shelf-life and the age of theother near the end of shelf-life) - Stability of solvent: long-term and accelerated & its protocol of 3 (pilot orproduction scale) batches (If applicable). - **Photo-stability study** on at least one pilot scale batch. **For Biosimilar products**: Side-by-side accelerated and stress studies carried out using a representative number of batches, comparing the biosimilar product to the reference product are mandatory to determine the similarity of the products by showing comparable degradation profiles. Anydifferences concerning the stability profile of the biosimilar product when compared to the reference product should be justified.		
19	**<u>- The stability studies must be performed as follows:</u>** - On the exact composition as that in the submitted CPP. - Carried out in the intended commercial drug product container-closuresystem - Contain name of the manufacturing site & primary packager - Contain manufacturing date (within 5- 10 years) - Contain tested parameters that follow specifications as in CTD section"3.2.P.5.1". - If finished product has more than one strength, container type or size, stability study must be done on 3 batches (in case of new registration) or one batch (in case of renewal) for each individual strength, container type orsize, unless bracketing is applied. - If FP has more than one manufacturer/ primary packager, all stabilitystudies must be submitted from each manufacturer/ primary packager. - Stability studies should include samples maintained in the inverted orhorizontal position (i.e., in contact with the closure), as well as in the upright position. (worst scenario) - If the scale of batches (production / pilot) is not stated in the CTD, then asigned and stamped declaration is needed to clarify the scale of the submitted batches. - Pilot scale batches can be provided with a commitment from the mother company to place the first three production scale batches into the long-termstability program after approval and submitting the study once completed - mentioning the date of submission in the commitment and batch numbers(in case of on-going stability on production batches). - The stability protocol used for studies on production scale batches shouldbe the same as that for the pilot batches, unless otherwise scientifically justified. - For imported products from non-reference countries only: Assay chromatograms should be submitted for each time point (in case of HPLCanalysis) or (last time interval by HPLC in case of any other method of analysis) for all batches included in all stability studies.		

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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

D. Requirements for Inspection and Stability file of Local BiologicalProducts			
20	**A. Administrative documents:** 1. Summary sheet (Word) + signed & stamped pdf. 2. Payment receipts 3. Certificate of responsibility stamped from the site at which the stability study was performed (signed by Q.C. analyst, Q.C. Head & Q.A Head). ➢ In case of performing the stability study in place rather than the manufacturer, attach the following: - Contract between the applicant and the place at which the stability study was performed (Authenticated by the legal counsel of EDA) - Copy of the license of the place at which the stability study was performed. **B. Requirements for finished product:** 1. Composition: ➢ Stamped and signed on applicant paper ➢ Mentioning trade name, dosage form, strength ➢ Mentioning function, reference to standard & grades (if applicable) of each ingredient. 2. Description of Manufacturing Process and Process Controls (name, dosage form) 3. Certificate of analysis "C.O. A" of 3 batches (Same as stability batches) of finished product (and solvent, if applicable): ➢ Signed and Stamped ➢ It should mention trade name, strength, dosage form, pack size & description, the manufacturer & primary packager. ➢ With manufacturing & expiry dates (corresponds to the required shelf life) and tested parameters as stated in specifications submitted in the file. ➢ If the product is powder: the color of powder before & after reconstitution should be mentioned in the COA and specifications. 4. Declaration with the shelf-life & storage conditions of the product: ➢ Signed &stamped from the manufacturer and to use the same wording of the proposed conditions as the reference product insert marketed in Egypt. ➢ In case of storage temperature at (25 °C): an undertaking by the applicant to store the product in warehouses and pharmacies at temperature not exceeding (25 °C) is required. 5. Pack description: ➢ Signed &stamped from the manufacturer ➢ Mentioning color, material of each component of primary pack, no. of units per secondary pack & its description. 6. Sampling record (محضر السحب), include the following: ➢ Batch no. (same as in stability study) ➢ Batch scale (pilot or production) ➢ Manufacturing date of batches 7. Reference product insert marketed in Egypt. 8. Sample.		

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البـريد الإلكـتـرونـي: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

9. Finished product specification:
   - Tested parameters: Appearance and description, Identity, Purity and impurities, Potency, Sterility test or alternatives, etc….
   - Mentioning method of analysis and reference for each method.
   - Justification of specification
10. Method of analysis. (detailed procedures)
11. Validation of analytical procedure of active substance assay and related substances along with HPLC chromatograms for each parameter (in case of HPLC analysis)
12. Stability Studies:

a) Stability Summary and Conclusion
   - ⇨ Summarizing the following details for each study (Long-term, accelerated, In-use, after reconstitution, after dilution, photostability or solvent):
     - Storage conditions (temperature & relative humidity) and duration of the study.
     - Details of tested batches (Manufacturing date, manufacturer & primary packager of finished product, pack details, batch scale (pilot or production))
     - Study protocol in tabular format (Tested attributes as per specifications and the frequency of testing for each test)
     - Summary of test results and justification for any out-of-specification results.
     - Conclusion for shelf-life and storage conditions.

b) Post-approval Stability Protocol and Stability Undertaking.
   - In case of issuing stability approval for pilot scale batches: an undertaking to place the first three production scale batches into the long-term stability program after approval and submitting the study once completed mentioning the date of submission in the undertaking.
   - The stability protocol used for studies on production scale batches should be the same as that for the pilot batches, unless otherwise scientifically justified.

c) Stability Data Tables and assay chromatograms for each time point (in case of HPLC analysis) or (last time interval by HPLC in case of any other method of analysis) for all batches included in all stability studies:
   - Each table should include the study type (long-term, accelerated, In-use, after reconstitution, after dilution, photostability), trade name & strength, batch number and pack size.
   - The shelf-life will be based on the stability data submitted (12 months data = shelf-life of 12 months, 18 months data = shelf-life of 18 months….etc.).

- N.B:
  - In case of more than one manufacturer, all stability studies must be submitted from each manufacturer.

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البـريد الإلكـتـرونـي: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

- Pilot scale batches can be provided with an undertaking by the manufacturer to place the first three production scale batches into the long-term stability program after approval and submitting the study once completed mentioning the date of submission in the undertaking.
- The stability protocol used for studies on production scale batches should be the same as that for the pilot batches, unless otherwise scientifically justified.
- Required number of batches for each study:

1- Long-term and accelerated studies on 3 (pilot or production) batches.
2- In-use :(after opening / after reconstitution / after dilution) stability study on at least two pilot scale batches. (The age of one batch is at the beginning of shelf-life and the age of the other near the end of shelf-life).
3- Photo-stability study on at least one pilot scale batch.
4- Long-term stability study of solvent on 3 (pilot or production) batches.
   - The stability studies must be performed on the exact composition as that attached to transfer letter
   - In case of the finished product has more than one strength, container type or size, stability study must be done on 3 batches for each individual strength, container type or size, unless bracketing is applied.
   - In case of more than one manufacturer, all stability studies must be submitted from each manufacturer (except photo-stability study).

- Additional studies in case of biosimilar product: Side-by-side accelerated and stress studies carried out using a representative number of batches, comparing the biosimilar product to the reference product are mandatory to determine the similarity of the products by showing comparable degradation profiles. Any differences concerning the stability profile of the biosimilar product when compared to the reference product should be justified.

C. Requirements for the active substance:

1- موافقة استيرادية سارية Valid importation permit
2- An undertaking letter from the applicant mentioning:
   - Active substance manufacturer name & full address
   - Batch number of finished product batches.
3- Stability testing site: If not stated in Manufacturers section in CTD or if more than one stability testing site is mentioned then a signed & stamped declaration from the MAH/manufacturer clarifying the stability testing site is required.
4- A declaration letter from the active substance manufacturer clarifying:
   - The stability testing site (name & address) mentioning API batch numbers.
5- Full S-Part from Module 3.
6- An undertaking by the applicant that the submitted S-Part is authentic & accurate.(تعهد صحة البيانات)

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البـريد الإلـكـتـرونـي: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

	7- C.O.A of recently manufactured active substance: ➢ Clarifying the manufacturer name & address ➢ With manufacturing & expiry dates (corresponds to the required shelf life) and tested parameters following the same specifications as in section "3.2.S.4.1". 8- Stability Study: ➢ Stability studies "3.2.S.7.3"and assay chromatograms for each time point (in case of HPLC analysis) or (last time interval by HPLC in case of any other method of analysis) for all batches included in all stability studies (for all batches included in all stability studies): - Long-term and accelerated stability studies and its protocol of 3 (pilot or production) batches carried out in the intended active substance container-closure system, containing manufacturing site, manufacturing date and tested parameters that follow the same specifications as in section "3.2.S.4.1", unless otherwise justified. N.B: ➢ In case of more than one manufacturer, all stability studies must be submitted from each manufacturer. ➢ Pilot scale batches can be provided with an undertaking by the manufacturer to place the first three production scale batches into the long-term stability program after approval and submitting the study once completed mentioning the date of submission in the undertaking and batch numbers (in case of on-going stability on production batches). ➢ The stability protocol used for studies on production scale batches should be the same as that for the pilot batches, unless otherwise scientifically justified.		

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
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التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

Unit Reception

File V : Scientific File Documents			
A- Administrative Part			
1	Product leaflet in case of first time approval/ approved insert in case of re-reg.		
2	International accreditation (EMA, FDA, TGA, MHLD/PMDA, WHO)		
3	Reference (BNF, Vidal, Compendium Swiss, Rote liste)		
4	Approved price or suggested price (only in cases of reliance file, fast track) &pricing receipt (signed and stamped on company Letter head)		
5	**if plasma derived product (plasma master file &viral inactivation)**		
6	Summary of product characteristics		
7	Scientific template (main and summary data)		
8	CD containing Module2 , Module 4 and Module 5 and contents of all the scientific dossier		
B-Plasma Master File			
1	Cover Letter (signed and stamped with all registered and under registrationproducts in Egypt)		
2	Health authority approval on plasma master file		
3	Certificate of plasma release from national regulatory released same year ofPMF submission.		
4	Service considerations		
5	Soft copy of Plasma Master File		
6	For imported finished blood products containing plasma from non-reference countries (not holding GMP from ref. countries or from recognized international accreditation (PPTA/IQPP)): EDA inspection approval for collection centers & finished product factory should be submitted.		

C- Package leaflet			
<u>In Case of imported reference country</u>			
Innovator products			
1	<u>Proposed</u> English Insert marketed in Country of Origin (Numbered)		
2	<u>Proposed</u> translated Arabic Insert, translated from a Certified translation office, except (Vaccines- Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one)		
3	SmPC "summary of product characteristics" and/or CCDS "companycore data sheet"		
4	Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert)		
5	Declaration from <u>MAH</u> that the submitted insert is the most updated & marketed in COO (insert status)		
6	Module 2-5 soft copy (In case of insert update)		
Biosimilar products			

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البريد الإلكتروني: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

Unit Reception

1	Proposed English Insert marketed in Country of Origin (Numbered)		
2	Proposed translated Arabic Insert, translated from a Certified translation office, except (Vaccines- Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one)		
3	Innovator product insert		
4	SmPC "summary of product characteristics" and/or CCDS "company core data sheet"		
5	Declaration from MAH that the submitted insert is the most updated & marketed in COO (insert status)		
6	Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert)		
7	Module 2-5 soft copy (In case of insert update)		
In case of imported product from non-reference country			
Standalone product:			
1	Proposed English Insert marketed in Country of Origin (Numbered)		
2	Proposed translated Arabic Insert, translated from a Certified translation office, except (Vaccines- Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one)		
3	SmPC "summary of product characteristics" and/or CCDS "company core data sheet"		
4	Declaration from MAH that the submitted insert is the most updated & marketed in COO (insert status)		
5	Reference model insert نموذج النشرة المرجعي التى قامت الشركة بكتابة نشرتها بناءاً عليه		
6	Scientific reference (Trials & Literature) : المرجع العلمي لكافة البيانات العلمية المذكورة بالنشرة من خلال الدراسات التى قامت بها الشركة او/و literatures		
7	Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert)		
8	Module 2-5 soft copy (In case of insert update)		
Biosimilar Product			
1	Proposed English Insert marketed in Country of Origin (Numbered)		
2	Proposed translated Arabic Insert, translated from a Certified translation office, except (Vaccines- Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one)		
3	SmPC "summary of product characteristics" and/or CCDS "company core data sheet"		
4	Declaration from MAH that the submitted insert is the most updated & marketed in COO (insert status)		
5	Reference model insert نموذج النشرة المرجعي التى قامت الشركة بكتابة نشرتها بناءاً عليه		
6	Scientific reference (Trials & Literature) : المرجع العلمي لكافة البيانات العلمية المذكورة بالنشرة من خلال الدراسات التى قامت بها الشركة او/و literatures		
7	Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert)		
8	Innovator product insert		
9	Module 2-5 soft copy (In case of insert update)		
In case of local products			
1	Proposed English Insert (Numbered)		
2	Proposed translated Arabic Insert, translated from a Certified translation office, except (Vaccines-		

العنـــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البريد الإلكتروني: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــون: ٠٢٣٧٤٨٤٩٨٨

	Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one)		
3	SmPC "summary of product characteristics"		
4	Reference model insert نموذج النشرة المرجعي التى قامت الشركة بكتابة نشرتها بناءاً عليه		
5	Scientific reference (Trials & Literature): المرجع العلمي لكافة البيانات العلمية المذكورة بالنشرة من خلال الدراسات التى قامت بها الشركة و/او ال literatures		
6	Declaration from MAH that the submitted insert is the most updated (insert status, mention revision date)		
7	Innovator product insert (in case of biosimilar)		
8	Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert)		
9	Comparative table between current & proposed insert and scientific reference for every part in the insert		
10	Module 2-5 soft copy (In case of insert update)		
	D- Albumin used as stabilizer Requirements		
1	EMA Approval if the plasma master file has an approval from EMA		
2	Certificate of batch release of health authority for this albumin used as astabilizer.		
3	Declaration from the MAH declares the trade name of the albumin used as astabilizer.		
4	**GENERAL INFORMATION (SUMMARY)** 1- Plasma-Derived Products' List 2- Overall Safety Strategy 3- General Logistics		
5	**TECHNICAL INFORMATION ON STARTING MATERIALS** 1- PLASMA ORIGIN 2- Information on centers or establishments in which blood/ plasmacollection is carried out, including inspection and approval, and epidemiological data onblood transmissible infections 3- Information on centers or establishments in which testing of donationsand plasma pools is carried out, including inspection and approval status 4- Selection/exclusion criteria for blood/plasma donors 5- System in place which enables the path taken by each donation to be traced from the blood/plasma collection establishment through to finishedproducts and vice versa		
6	**Plasma Quality and Safety** 1 Compliance with European Pharmacopoeia Monographs. 2 Testing of blood/plasma donations and pools for infectious agents, including information on test methods and, in the case of plasma pools, Validation data on the tests used.		
7	Technical characteristics of bags for blood and plasma collection, including information on anticoagulant solutions used.		

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البريد الإلكتروني: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

Unit Reception

			check Notes
File VI- PV requirements			
A- Imported products (Soft copy searchable text PDF should be provided)			
1	Delegation letter "خطاب التفويض"		
2	Updated Cover letter (on the company paper of the PV representative/agent/scientific office) clarifying the Date of the submission (not exceeding 2 days before the submission)/ Directed to the Manager of General Administration of Pharmaceutical Vigilance/ Name of the product /Name of the Active substance/ context of submission/ Name of the MAH/ Content of the submission/ Actual signature of the QPPV or LSR "signature by QPPV or LSR (not print screen)"- "Accepted Digital/Electronic signature"/company stamp		
3	صورة ضوئية من أصل ايصال سداد + "pink receipt" صورة ضوئية. من أصل ايصال سداد "yellow receipt" لكل **(Application number)** مقابل الخدمات المقدمة من الادارة المركزية للرعاية الصيدلية مختوم ا بختم اليقظة بقيمة ١٠٠٠ جنيه مصري "لا تشمل ضريبة القيمة المضافة" عن طلب تقييم التقرير/ التقارير المجمعة الدورية لمأمونية المستحضر (PSUR) طبقا لقرار السيد الاستاذ الدكتور رئيس الهيئة رقم ٢٠٢٢/٩٩		
4	صورة ضوئية من أصل ايصال سداد + "pink receipt" صورة ضوئية من أصل ايصال سداد "yellow receipt" لكل **(Application number)** مقابل الخدمات المقدمة من الادارة المركزية للرعاية الصيدلية مختوم ا بختم اليقظة بقيمة ١٠٠٠ جنيه مصري "لا تشمل ضريبة القيمة المضافة" عن طلب تقييم خطة إدارة المخاطر (RMP) طبقا لقرار السيد الاستاذ الدكتور رئيس الهيئة رقم ٦ / ٢٠٢١ (موضحا بالايصال اسم المستحضر/المادة الفعالة/التركيز – الشكل الصيدلي/اطار التقديم/ اسم الشركة صاحبة المستحضر)		
5	Confirmation e-mail by PSMF reception portal (as an evidence of submission of the PSMF of the company to EPVC) **OR** Latest released valid PSMF assessment report "for all concerned parties"		
6	Updated version of Summary of PSMF(s)/PSSF		
7	In case of submission by PV representative or agent, the PV rep./agent should submit an authorized and authenticated (by all concerned parties) PV agreement between the MAH & the service provider covering all the PV activities including the concerned product(s) N.B: Starting form 15/05/2022, EPVC will not receive the PV agreement without the inclusion of the concerned product."		
8	The latest Periodic Safety Update Report (PSUR) in PSUR format "as per GVP for Arab Countries V.2.0" covering at least the last 3 years OR separate PSURs covering at least the last 3 years.		
9	The most updated "EU/Global/Core-Risk Management Plan (RMP)"of the product.		
10	The Egyptian display of EU-RMP		
B- Local products (Soft copy searchable text PDF should be provided)			
1	Delegation letter خطاب تفويض		
2	Updated Cover letter (on the company paper of the PV representative/agent/scientific office) clarifying the Date of the submission (not exceeding 2 days before the submission)/ Directed to the Manager of General Administration of Pharmaceutical Vigilance/ Name of the product /Name of the Active substance/ context of submission/ Name of the MAH/ Content of the submission/ Actual signature of the QPPV "signature by QPPV (not print screen)"/company stamp		

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البريد الإلكتروني: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨

3	صورة ضوئية من أصل ايصال سداد + "pink receipt" صورة ضوئية من أصل ايصال سداد "yellow receipt" لكل (Application number) مقابل الخدمات المقدمة من الادارة المركزية للرعاية الصيدلية مختوم ا بختم اليقظة بقيمة ٥٠٠ جنيه مصري "لا تشمل ضريبة القيمة المضافة" عن طلب تقييم خطة إدارة المخاطر (RMP)طبقا لقرار السيد الاستاذ الدكتور رئيس الهيئة رقم ٦ / ٢٠٢١ (موضحا بالايصال اسم المستحضر/المادة الفعالة/التركيز – الشكل الصيدلي/اطار التقديم/ اسم الشركة صاحبة المستحضر)		
4	Confirmation e-mail by PSMF reception portal (as an evidence of submission of the PSMF of the company to EPVC) or Latest released valid PSMF assessment report "for all concerned parties"		
5	Updated version of Summary of PSMF(s)/PSSF		
6	In case of submission by PV representative, the PV rep should submit an authorized and authenticated (by all concerned parties) PV agreement between the MAH & the service provider covering all the PV activities including the concerned product(s) N.B: Starting form 15/05/2022, EPVC will not receive the PV agreement without the inclusion of the concerned product."		
7	Egyptian-Risk Management Plan (RMP)"of the product.		
8	The latest Periodic Safety Update Report (PSUR) in PBRER format of the imported ready to fill final bulk covering at least the last 3 years** صورة ضوئية من "pink receipt"+ وفي هذه الحالة يتعين على الشركة تقديم صورة ضوئية من أصل ايصال سداد ** "yellow receipt" أصل ايصال سداد لكل **(Application number)** مقابل الخدمات المقدمة من الادارة المركزية للرعاية الصيدلية مختوم ا بختم اليقظة بقيمة ١٠٠٠ جنيه مصري "لا تشمل ضريبة القيمة المضافة" عن طلب تقييم التقرير/ التقارير المجمعة الدورية لمأمونية المستحضر (PSUR) ٩٩ طبقا لقرار السيد الاستاذ الدكتور رئيس الهيئة رقم ٢٠٢٢/		

العنـــــــــــوان: ٥١ شارع وزارة الزراعة، العجوزة – الجيزة
البريد الإلكتروني: المكتب الفني / bio.tech@edaegypt.gov.eg، المكتب الإداري /bio.admin@edaegypt.gov.eg
التـــلـيـــفـــــون: ٠٢٣٧٤٨٤٩٨٨